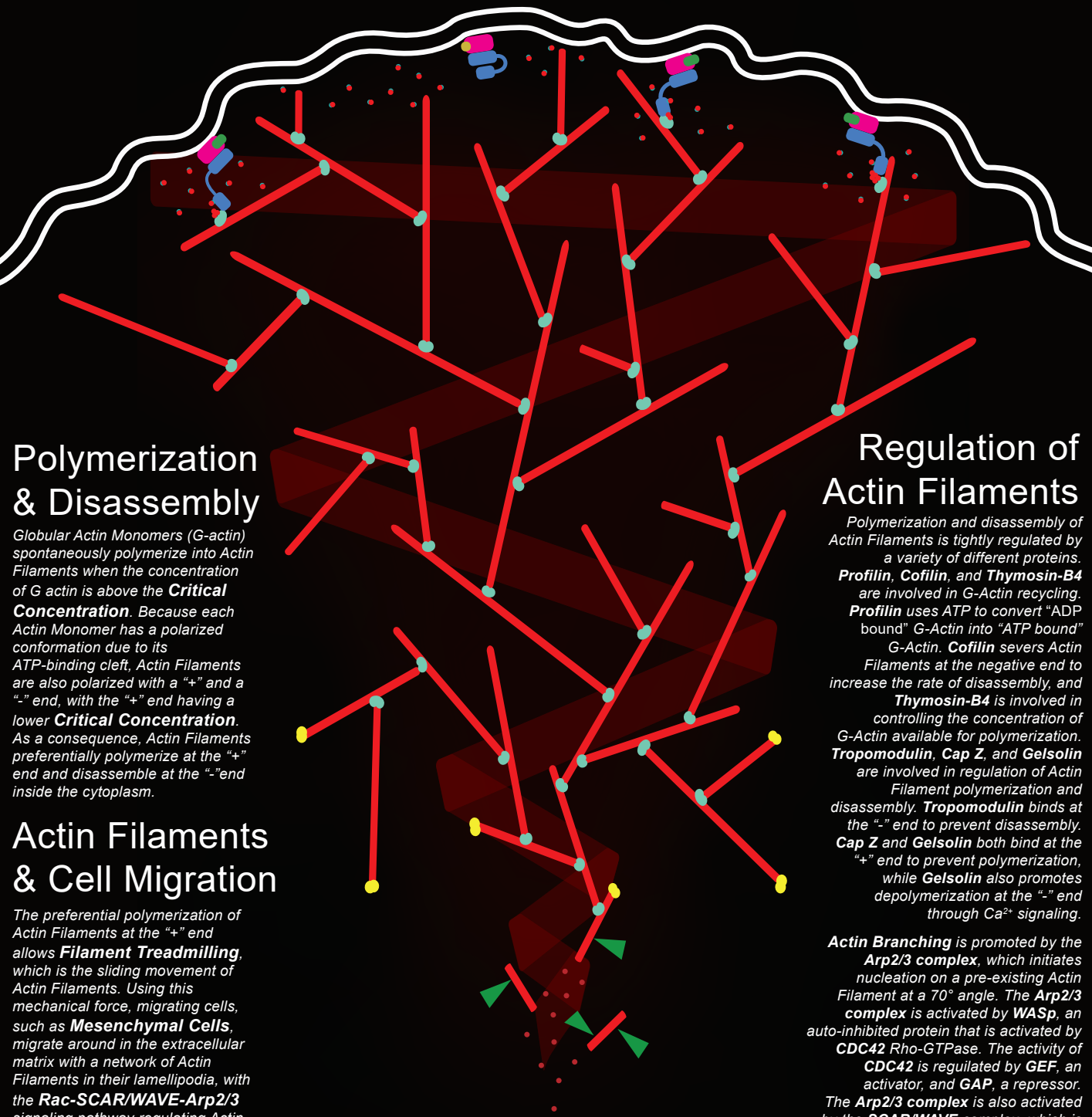
ACTIN

CYTOSKELETON AND CELL POLARITY



Polymerization & Disassembly

Globular Actin Monomers (G-actin) spontaneously polymerize into Actin Filaments when the concentration of G actin is above the ***Critical Concentration****. Because each Actin Monomer has a polarized conformation due to its ATP-binding cleft, Actin Filaments are also polarized with a "+" and a "-" end, with the "+" end having a lower* ***Critical Concentration****. As a consequence, Actin Filaments preferentially polymerize at the "+" end and disassemble at the "-"end inside the cytoplasm.*

Actin Filaments & Cell Migration

The preferential polymerization of Actin Filaments at the "+" end allows ***Filament Treadmilling****, which is the sliding movement of Actin Filaments. Using this mechanical force, migrating cells, such as* ***Mesenchymal Cells****, migrate around in the extracellular matrix with a network of Actin Filaments in their lamellipodia, with the* ***Rac-SCAR/WAVE-Arp2/3*** *signaling pathway regulating Actin Polymerization and Branching.*

Regulation of Actin Filaments

Polymerization and disassembly of Actin Filaments is tightly regulated by a variety of different proteins. ***Profilin****,* ***Cofilin****, and* ***Thymosin-B4*** *are involved in G-Actin recycling.* ***Profilin*** *uses ATP to convert* "ADP bound" *G-Actin into "ATP bound" G-Actin.* ***Cofilin*** *severs Actin Filaments at the negative end to increase the rate of disassembly, and* ***Thymosin-B4*** *is involved in controlling the concentration of G-Actin available for polymerization.* ***Tropomodulin****,* ***Cap Z****, and* ***Gelsolin*** *are involved in regulation of Actin Filament polymerization and disassembly.* ***Tropomodulin*** *binds at the "-" end to prevent disassembly.* ***Cap Z*** *and* ***Gelsolin*** *both bind at the "+" end to prevent polymerization, while* ***Gelsolin*** *also promotes depolymerization at the "-" end through* Ca^{2+} *signaling.*

Actin Branching *is promoted by the* ***Arp2/3 complex****, which initiates nucleation on a pre-existing Actin Filament at a 70° angle. The* ***Arp2/3 complex*** *is activated by* ***WASp****, an auto-inhibited protein that is activated by* ***CDC42*** *Rho-GTPase. The activity of* ***CDC42*** *is regulated by* ***GEF****, an activator, and* ***GAP****, a repressor. The* ***Arp2/3 complex*** *is also activated by the* ***SCAR/WAVE*** *complex, which is regulated by* ***Rac****, a small GTPase*

DYNAMICS & REGULATION

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